EXPRESS MAIL NO. EV335607987US

EXPRESS ABANDONMENT UNDER 37 CFR 1.138

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Application Number	09/847,519
Filing Date	May 1, 2001
First Named Inventor	Ralf M. Luche
Art Unit	1652
Examiner Name	NASHED, Nashaat T.
Attorney Docket Number	200125.422

Please **check only one** of boxes 1 or 2 below:
(If no box is checked, this paper will be treated as a request for express abandonment as of the filing date of this paper.)

1. [X] **Express Abandonment**
I request that the above-identified application be expressly abandoned as of the filing date of this paper.

Applicants respectfully submit that by filing the instant express abandonment Applicants are not acquiescing to any rejection(s) or objection(s) pending in any Official Action or Advisory Action in the above-identified patent application. Further, Applicants respectfully traverse any and all outstanding rejections.

2. [ ] **Express Abandonment in Favor of a Continuing Application**
I request that the above-identified application be expressly abandoned as of the filing date accorded the continuing application filed previously herewith.

NOTE: A paper requesting express abandonment of an application is not effective unless and until an appropriate USPTO official recognizes and acts on the paper. See the Manual of Patent Examining Procedure (MPEP) 711.01.

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I am the:
- [ ] applicant.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration No. **48,903**
- [ ] attorney or agent acting under 37 CFR 1.34(a) (may act under 37 CFR 1.34(a) only if box 2 above, stating that the application is expressly abandoned in favor of a continuing application, is checked). Attorney or agent registration number if acting under 37 CFR 1.34(a).

(Attorney or agent registration number)

Mae Joanne Rosok — Signature

May 11, 2004 — Date

Mae Joanne Rosok — Typed or printed name

206-622-4900 — Telephone Number

Note: Signatures of all the inventors or assignees of record of the entire interest or their representatives(s) are required. Submit multiple forms if more than one signature is required, see below.

[ ] Total of ____ forms are submitted.

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EXPRESS MAIL NO. EV335607987US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Ralf M. Luche and Bo Wei
Application No.	:	09/847,519
Filed	:	May 1, 2001
For	:	DSP-14 DUAL-SPECIFICITY PHOSPHATASE
Examiner	:	NASHED, Nashaat T.
Art Unit	:	1652
Docket No.	:	200125.422
Date	:	May 11, 2004

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REMARKS REGARDING EXPRESS ABANDONMENT UNDER 37 C.F.R. § 1.138

Commissioner for Patents:

We respectfully submit the following remarks in response to the Advisory Action mailed February 9, 2004 by the U.S. Patent and Trademark Office (PTO). A Notice of Appeal was filed on January 12, 2004; accordingly, please extend the period for response by two (2) months, to expire on May 12, 2004.

REMARKS

We respectfully submit the following remarks. Claims 6-10 and 12-14 are currently pending.

The PTO rejects claims 6-10 and 12-14 under 35 U.S.C. § 101, alleging that the claimed polynucleotide lacks a specific, substantial, and credible utility and a well-established utility, and under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Applicants traverse these rejections and, for reasons already made of record (*see* Responses submitted August 6, 2002, June 4, 2003, and January 12, 2004), submit that the PTO has failed to set forth a *prima facie* case showing that the subject matter of the instant claims lacks utility. Applicants further submit that as described in the present specification and the instant claims, Applicants enabled a skilled artisan to make and use the claimed polynucleotides at the time the Application was filed.

Applicants have presented factual findings and sound scientific reasoning, not conclusory statements as asserted in the Advisory Action, that a person having ordinary skill in the art would reasonably conclude that the claimed polynucleotides and the encoded polypeptide products have a specific, substantial, and credible utility. The presently claimed subject matter relates to isolated polynucleotides that encode a dual specificity phosphatase polypeptide (DSP-14) having a conserved dual specificity phosphatase active site and a high homology to known, enzymatically active members of the dual specificity phosphatase family. Moreover, phosphatase activity of a DSP-14 polypeptide encoded by the claimed polynucleotides has been demonstrated as described in the Declaration of Dr. Ralf Luche, which was submitted January 12, 2004 with the Response to the Final Office Action (mailed August 12, 2003).

The claimed DSP-14-encoding polynucleotides and the DSP-14 polypeptide products have a specific and substantial utility that a person skilled in the art would find credible, based on the skilled artisan's knowledge regarding regions of conserved sequence homologies that are present in dual specificity phosphatases, and which conserved homology regions are present in DSP-14. The specification teaches that the conserved protein tyrosine phosphatase active site motif (-C-X_5-R-) is contained within the DSP-14 polypeptide encoded by the

presently claimed polynucleotides, and that in DSP-14 this motif comprises the peptide sequence VHCVMGRSRSATLVLAYLM (SEQ ID NO:3). (*See, e.g.,* specification page 8, lines 24-25; page 13, lines 1-2; SEQ ID NO:2 at amino acid positions 145-163). Because conserved PTP catalytic site motifs are well known in the PTP art, a skilled artisan would readily believe that Applicants have discovered a new member of the dual specificity phosphatase family. (*See, e.g.,* instant specification, at page 46, lines 8-14; *see also* Keyes, *Biochim. Biophys. Acta* 1265:152-60; Fauman et al., *Trends in Biochem. Sci.* 21:413-17 (1996); Jia, *Biochem. Cell Biol.* 75:17-26 (1997); Flint et al., *Proc. Natl. Acad. Sci. USA* 94:1680-85 (1997); U.S. Patent No. 6,258,582, at column 13, lines 4-18; U.S. Patent No. 6,132,964 at column 13, lines 21-40 and SEQ ID NO:4 therein). (*See also* U.S. Patent Nos. 6,132,964 ('964) and 6,258,582 ('582)).

Applicants are puzzled by the PTO's repeated assertion that U.S. Patent Nos. 6,258,582 ('582) and 6,132,964 ('964) do not support the substantial, specific, and credible utility of the dual specificity phosphatase described in the instant Application. As pointed out by Applicants, for instance in the Response submitted January 12, 2004, the Application teaches that DSP-14 is a dual specificity phosphatase and that "[d]ual-specificity protein tyrosine phosphatases (dual-specificity phosphatases) are phosphatases that dephosphorylate both phosphotyrosine and phosphothreonine/serine residues (Walton et al., *Ann. Rev. Biochem.* 62:101-120, 1993)." (Page 2, lines 5-7). This sentence explicitly states what are the particular phosphorylated amino acids from which a phosphate group is hydrolyzed by dual specificity phosphatases. Applicants therefore respectfully submit that the PTO errs in its assertion (Advisory Action, page 3, third paragraph) that the Application discloses dual specificity phosphatases belonging to " a distinct family of enzymes from those of Ser/Thr phosphatases and Tyr phosphatases," which the PTO seems to believe are described in the '582 and '964 patents.

Applicants respectfully point out that each of the '964 and the '582 patents describes a member of the dual specificity phosphatase (DSP) family. The DSP family members described therein hydrolyze a phosphate group on a tyrosine, serine, or threonine, like DSP-14, and have a PTP active site motif (-C-X_5-R-). The '964 patent discloses that HHLM-4 (SEQ ID NO:4 therein) "has a *tyrosine protein phosphatase active site signature sequence* V146 through L158" (VHCAVGVSRSATL) (*see* column 13, lines 24-25; SEQ ID NO:4, emphasis added;

active site motif underlined) and "has chemical and structural homology with a human *dual-specificity protein phosphatase*" (column 13, lines 29-31, emphasis added). Similarly, '582 discloses a dual specificity phosphatase that is capable of catalyzing the removal of a phosphate group attached to a tyrosine, serine, or threonine residue of a protein or polypeptides (*e.g.*, a phosphoprotein) (column 9, lines 52-61). '582 further teaches that the polypeptides disclosed therein contain an extended catalytic active domain (VXVHCXAGXSRSXTX(3)AYLM) (active site motif underlined), which is capable of facilitating the removal of a phosphate group attached to a tyrosine, serine, or threonine residue of a phosphoprotein ('582, column 12, lines 35-38; see also, column 25, lines 18-25).

The PTO further asserts that the claimed polynucleotides encoding a DSP-14 polypeptide lack utility because a homologous sequence disclosed in U.S. Patent No. 6,268,135 ('135, Acton) is allegedly a phospholipase. Dr. Luche's expert opinion regarding the polypeptide having the sequence set forth in SEQ ID NO:2 disclosed in '135 is hardly mere speculation, as asserted by the PTO, but is founded upon logical, scientific reasoning based upon his knowledge in the art and the facts disclosed in '135. The facts disclosed in '135 include the following: (1) the PTP catalytic site motif -C-X_5-R- can be found at positions 138-144 of SEQ ID NO:2 disclosed therein; (2) the '135 patent teaches that the polypeptide (SEQ ID NO:2, '135) is similar to dual specificity protein phosphatase 3 (Accession No. P51452, approximately 37% identical over amino acids 1-199 of CSAPL) (column 56, lines 19-29); (3) the phospholipase A_2 active site includes the consensus sequence CCX_2HX_2C ('135, at column 7, lines 60-65); (4) the polypeptide amino acid sequence disclosed in '135 (SEQ ID NO:2) does *not* possess a phospholipase A_2 active site located at amino acid positions 131-138 of that sequence (column 8, lines 3-6); and (5) *no* portion of SEQ ID NO:2 disclosed therein includes the phospholipase A_2 active site motif.

The PTO asserts that Dr. Luche bases his conclusions regarding the catalytic activity of SEQ ID NO:2 disclosed in the '135 patent without "experimental facts." In view of the facts disclosed in '135, however, absolutely no scientific rationale exists for Dr. Luche or for any other artisan skilled in the PTP arts to perform an experiment that assesses phospholipase activity of a polypeptide that *does* contain a PTP active site motif but that *does not* contain a

phospholipase A_2 active site motif. A skilled artisan, as evidenced by the Declaration of Dr. Luche, could not reasonably conclude that the presently claimed polynucleotides might encode a polypeptide with phospholipase activity on the basis of the disclosure in '135; therefore, the '135 patent would not lead a skilled artisan to doubt Applicants' asserted utility of the claimed invention. The PTO's assertion that '135 would lead a skilled artisan to conclude otherwise because the patent is presumed valid is an assertion of form, wholly without substance.

Moreover, Applicants have provided the PTO with evidence that the claimed polynucleotides encode an enzymatically active dual specificity phosphatase polypeptide (*see* Declaration of Dr. Luche submitted January 12, 2004). The PTO has chosen to disagree with the Declaration submitted by an expert, and alleges in the Advisory Action that "the 6,8-difluoro-4-methylumbelliferyl phosphate substrate cannot distinguish between a protein phosphatase and a phospholipase, or any other phosphatase activity." (*See* Action at page 3, first paragraph). This conclusory assertion lacks scientific merit. Because a phosphatase hydrolyzes phosphate monoesters to an alcohol and inorganic phosphate, and a phospholipase A_2 enzyme catalyzes the release of fatty acids from the second carbon group of a glycerol of a phospholipid, an artisan skilled in either the PTP art or the phospholipase art would be surprised to find that a phosphatase substrate having no activity as a phospholipase substrate would not distinguish between the two activities. In fact, MUP, the molecule from which 6,8-difluoro-4-methylumbelliferyl phosphate substrate was derived, has been used for many years to identify protein phosphatase activity (*see, e.g., J. Immunol. Methods* 150:23 (1992) and references cited therein). Furthermore, the 6,8-difluoro-4-methylumbelliferyl phosphate substrate was derived to increase the sensitivity for detecting protein phosphatases, and additional assays have been developed to distinguish protein tyrosine phosphatase activity from serine/threonine phosphatase activity (*see* Gee et al., *Anal. Biochem.* 273:41-48 (1999); Pastula et al., *Comb. Chem. High Throughput Screen.* 6:341-46 (2003)). (For phospholipase substrates, see, for example, Molecular Probes, Invitrogen Life Technologies, Eugene, OR; sections 18.3 and 18.4 of Resource Material).

With regard to enablement, Applicants submit that the instant specification provides sufficient disclosure to teach a person having ordinary skill in the art how to make and

use the claimed invention. For reasons already made of record, the specification discloses the polynucleotide sequence (SEQ ID NO:1) that encodes a DSP-14 polypeptide (*see* SEQ ID NO:2) and discloses that the DSP-14 polypeptide is capable of dephosphorylating a DSP-14 substrate (*see, e.g.,* page 6, line 25 through page 7, line 3). As taught in the instant Application and presented in the Declaration submitted on January 12, 2004, the claimed DSP-14 polynucleotide may be inserted into an expression vector that is transfected into a host cell to produce the DSP-14 polypeptide (*see, e.g.*, page 9, line 8 through page 10, line 2). The expressed polypeptide can then be analyzed for its ability to dephosphorylate a suitable substrate according to assays for detecting DSP-14 activity, which are also described in the specification (*see, e.g.,* page 18, line 1 through page 19, line 24) and in the Declaration. In addition, the specification enables the cloning and expression of DSP-14 substrate trapping mutants, which may be used for characterizing and identifying DSP-14 substrates and for identifying agents that alter intracellular molecular signaling by modulating DSP-14 activity. (*See, e.g.*, at page 7, line 12 through page 8, line 5; page 37, line 7 through page 40, line 12). Applicants submit that all of the aforementioned methods may be performed by permissible routine screening and without undue experimentation.

Applicants also note, with some puzzlement, that the Advisory Action (bottom of page 3) alleges with regard to page 5, second paragraph, of Applicants' Response submitted January 12, 2004, that "applicant elude [*sic*] to a declaration that will address U.S. patent 6,268,135. There is no declaration accompanied [*sic*] applicants [*sic*] response." Applicants respectfully point out that at no place on page 5 of the Response is a reference made to a Declaration; other pages of the Response do refer to the Declaration of Dr. Luche, which, as noted above, was in fact submitted to the PTO on January 12, 2004, along with the Response. The PTO must concede that the Declaration was received because it is referred to repeatedly in the Advisory Action, including reference to Dr. Luche's comments regarding '135. The Declaration was also acknowledged on the postcard that was included with Applicants' submission of January 12, 2004, which postcard was date-stamped by the PTO mailroom (copy enclosed).

In view of the foregoing and also for reasons previously made of record, Applicants respectfully submit that the claimed invention has a well-established and specific, substantial, and credible utility, which satisfies the requirements of 35 U.S.C. § 101. Applicants further submit that the specification enables a person having skill in the art to make and use the claimed invention in full compliance with 35 U.S.C. § 112, first paragraph.

Nevertheless, Applicants request that the present Application be expressly abandoned under 37 C.F.R. § 1.138, according to the Express Abandonment submitted herewith.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

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Enclosures:

Express Abandonment
Petition for Extension of Time
Copy of date-stamped postcard included with Response submitted January 12, 2004

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